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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/550,072 | WINICOV, ILGA | |
| | Examiner | Art Unit | |
| | Cynthia Collins | 1638 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *June 23, 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *51109*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

The Amendment filed June 23, 2009 has been entered.

Claims 1-3 and 6-9 are currently amended.

Claims 1-9 are pending.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-9 require the presence or use of a genus of nucleotide sequences of unspecified structure that have the designation "a MsPRP2 secretion signal", and are part of an expression cassette.

The specification describes expression cassettes that comprise " a fragment of the MsPRP2 promoter and signal sequence (-652 to +75), where +1 is the A of ATG start of the

MsPRP2 coding sequence (Bastola et al., 1998)", the sequence of which is depicted in Fig. 3. Accordingly, the specification describes a single species of the required genus of sequences, the sequence corresponding to +1 to +75 of the nucleotide sequence depicted in Fig. 3. The specification does not describe other sequences that have the designation "a MsPRP2 secretion signal".

The Federal Circuit has clarified the application of the written description requirement to nucleotide sequences. The court stated that "A description of a genus of cDNAs may be achieved by means of recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." See *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1569; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court has also affirmed the PTO's applicable standard for determining compliance with the written description requirement, quoting from the PTO's Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, P1, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106, where it is set forth that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ... i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." See *Enzo Biochem Inc. v. Gen-Probe Inc.*, 63 USPQ2d 1609, 1613 (CAFC 2002)

In the instant case Applicant has not described a representative number of species falling within the scope of the genus of nucleotide sequences required by the rejected claims, which

sequences have the designation "a MsPRP2 secretion signal", or the structural features unique to the genus that are correlated with their function of protein secretion.

Claims 2-3 and 6-9 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the office action mailed March 30, 2009.

Applicant's arguments filed June 23, 2009 have been fully considered but they are not persuasive.

Applicant maintains that the claims are described because the MsPRP2 promoter is known and is disclosed in FIG. 2 Applicant also maintains that the claims are described because Alfin 1 is known. (reply pages 6-7)

Applicant's arguments are not persuasive because the claims are not limited to specific sequences that are known or disclosed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 9 remains rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps, for the reasons of record set forth in the office action mailed March 30, 2009.

Applicant's arguments filed June 23, 2009 have been fully considered but they are not persuasive.

Applicant maintains that the amendment of the claim should overcome the rejection.

Applicant's arguments are not persuasive because the mere recitation of an end result is not an essential step that would result in the bioremediation of the field.

Claims 1-3 and 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Winicov (WO 99/53016, published October 21, 1999) in view of Lee et al. (U.S. Patent No. 6,020,169, issued February 1, 2000) and Deutch C.E. et al. (Post-transcriptional regulation of a salt-inducible alfalfa gene encoding a putative chimeric proline-rich cell wall protein. Plant Mol Biol. 1995 Jan;27(2):411-8).

The claims are drawn to an expression cassette capable of directing heterologous protein expression in plant roots, comprising a) a MsPRP2 promoter or a fragment thereof, including a promoter or fragment comprising a portion of SEQ ID NO : 1; b) a MsPRP2 secretion signal; and c) nucleotides encoding a heterologous protein, operably linked to the MsPRP2 promoter.

The claims are also drawn to an expression cassette capable of directing heterologous protein expression in plant roots, comprising a) a MsPRP2 promoter or a fragment thereof, said promoter or fragment comprising a portion of SEQ ID NO : 1; b) a MsPRP2 secretion signal; and c) nucleotides encoding a heterologous protein, operably linked to the MsPRP2 promoter, said expression cassette further comprising nucleotides encoding transcription factor Alfin1, the nucleotides encoding Alfin1 being operably linked to another promoter such that the other promoter causes the transcription factor Alfinl to be overexpressed.

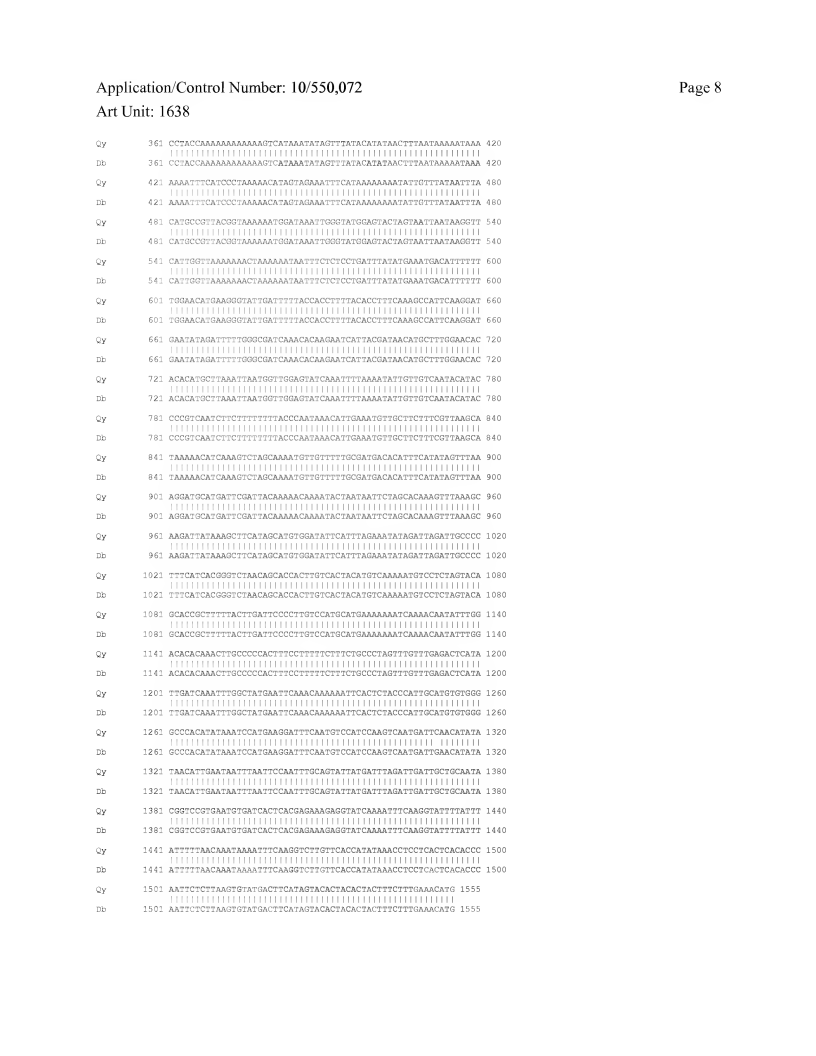
The claims are additionally drawn to a plant cell culture transfected with the expression cassette of claim 1.

The claims are further drawn to methods comprising: a. growing plant cells which have been transfected with an expression cassette comprising: i) a MsPRP2 promoter or a fragment thereof; and ii) nucleotides encoding a MsPRP2 secretion signal, wherein the nucleotides encoding the MsPRP2 secretion signal are downstream from the MsPRP2 promoter or fragment thereof; and iii) nucleotides encoding a protein, said nucleotides encoding the protein being operably linked to the MsPRP2 promoter, and b. growing the transformed cells, during which the transformed cells produce the protein.

Winicov teaches an expression cassette capable of directing heterologous protein expression in plant roots comprising an MsPRP2 promoter or a fragment thereof and "other genes" operably linked to the MsPRP2 promoter (paragraph spanning pages 19-20). The promoter or fragment thereof comprises a portion of SEQ ID NO : 1; see sequence alignment below. The "other genes" are genes for a "heterologous" protein because "other" genes are not the MsPRP2 gene from which the promoter was obtained.

```
RESULT 2
AAZ34539
ID   AAZ34539 standard; DNA; 1612 BP.
XX
AC   AAZ34539;
XX
DT   01-FEB-2000  (first entry)
XX
DE   Alfalfa salt inducible MsPRP2 gene promoter region.
XX
KW   MsPRP2 gene; promoter; Alfin1; transcription factor; alfalfa;
KW   salt tolerance; stress tolerance; transgenic plant; root; ds.
XX
OS   Medicago sativa.
XX
FH   Key             Location/Qualifiers
FT   protein_bind     complement(718. .727)
FT                   /*tag= a
FT                   /note= "Alfin1 binding site"
FT   protein_bind     complement(778. .786)
FT                   /*tag= b
FT                   /note= "Alfin1 binding site"
FT   protein_bind     complement(1034. .1049)
FT                   /*tag= c
FT                   /note= "Alfin1 binding site"
FT   protein_bind     complement(1079. .1087)
FT                   /*tag= d
```

```
FT                   /note= "Alfin1 binding site"
FT   protein_bind    complement(1155. .1160)
FT                   /*tag= e
FT                   /note= "Alfin1 binding site"
FT   protein_bind    1251. .1261
FT                   /*tag= f
FT                   /note= "Alfin1 binding site"
FT   CAAT_signal     1449. .1453
FT                   /*tag= g
FT   TATA_signal     1478. .1483
FT                   /*tag= h
FT   CDS             1553. .1612
FT                   /*tag= i
FT                   /partial
FT                   /note= "5' end of coding sequence"
XX
PN   WO9953016-A2.
XX
PD   21-OCT-1999.
XX
PF   08-APR-1999;    99WO-US007902.
XX
PR   09-APR-1998;    98US-0081348P.
PR   07-APR-1999;    99US-0128083P.
XX
PA   (UYAR-) UNIV ARIZONA STATE.
XX
PI   Winicov I;
XX
DR   WPI; 2000-013097/01.
XX
PT   Producing novel transgenic plants tolerant to a wide variety of biotic
PT   and abiotic stress conditions.
XX
PS   Claim 13; Fig 3; 21pp; English.
XX
CC   This is the nucleotide sequence of the promoter region of the root-
CC   directed salt-inducible MsPRP2 gene of alfalfa. The promoter includes
CC   potential sites for binding to Alfin1 (see AAY32183), a newly identified
CC   root-specific transcription factor of alfalfa that is associated with
CC   salt tolerance. The full or partial MsPRP2 promoter sequence can be used
CC   by itself or in conjunction with other promoter sequence elements to
CC   construct new composite promoter regulatory sequences that would give
CC   root-specific and/or Alfin1 protein regulated expression to other genes
CC   transferred into plants. The Alfin1 protein binding sequences could also
CC   be used, as concatenates or in conjunction with other promoter sequence
CC   elements, to construct new composite promoter regulatory sequences. It is
CC   believed the introduction of Alfin1 binding sites in appropriate promoter
CC   contexts could lead to regulation of additional genes by Alfin1. The
CC   invention may be used to manipulate plant growth and to enhance plant
CC   tolerance to a wide variety of biotic and abiotic stress conditions,
CC   including salt
XX
SQ   Sequence 1612 BP; 561 A; 274 C; 214 G; 563 T; 0 U; 0 Other;

  Query Match             99.9%;  Score 1553.4;  DB 1;  Length 1612;
  Best Local Similarity   99.9%;  Pred. No. 2.5e-228;
  Matches 1554;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 TTTTATAAATATTTAAGCTTGATAATAATTTTGCGATCTATATATAAGCCACTACCAATT 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 TTTTATAAATATTTAAGCTTGATAATAATTTTGCGATCTATATATAAGCCACTACCAATT 60

Qy         61 TAAAATTATATATATATATATATATATATATATATATATATAATAATTTTTATTATATTTAT 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TAAAATTATATATATATATATATATATATATATATATATATAATAATTTTTATTATATTTAT 120

Qy        121 TACGTTGATGGTAAAAAAATAAATATAATTTGTTACCATTTAAAAGTCATAAATATAGTA 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 TACGTTGATGGTAAAAAAATAAATATAATTTGTTACCATTTAAAAGTCATAAATATAGTA 180

Qy        181 CAATCCAACCCTTTGAGAGGTTAATGTGTGTGCGGATTTTCTAGATAAACAAGGTGCCAT 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 CAATCCAACCCTTTGAGAGGTTAATGTGTGTGCGGATTTTCTAGATAAACAAGGTGCCAT 240

Qy        241 TCACGATTCTTCTTGGTGCAGCTTGGAGAACCCTATCCTGGGCTTGGAAGATTTACTTCT 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 TCACGATTCTTCTTGGTGCAGCTTGGAGAACCCTATCCTGGGCTTGGAAGATTTACTTCT 300

Qy        301 TGTTGATGCTTCTAGAGTACAGCTCCTTAAGGCTGTAGTCTAGTTTTTTTTTTCATCCTT 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 TGTTGATGCTTCTAGAGTACAGCTCCTTAAGGCTGTAGTCTAGTTTTTTTTTTCATCCTT 360
```


Qy 361 CCTACCAAAAAAAAAAAAGTCATAAATATAGTTTATACATATAACTTTAATAAAAATAAA 420
Db 361 CCTACCAAAAAAAAAAAAGTCATAAATATAGTTTATACATATAACTTTAATAAAAATAAA 420
Qy 421 AAAATTTCATCCCCTAAAAACATAGTAGAAATTTCATAAAAAAAATATTGTTTATAATTTA 480
Db 421 AAAATTTCATCCCCTAAAAACATAGTAGAAATTTCATAAAAAAAATATTGTTTATAATTTA 480
Qy 481 CATGCCGTTACGGTAAAAAATGGATAAATTGGGTATGGAGTACTAGTAATTAATAAGGTT 540
Db 481 CATGCCGTTACGGTAAAAAATGGATAAATTGGGTATGGAGTACTAGTAATTAATAAGGTT 540
Qy 541 CATTGGTTAAAAAAACTAAAAAATAATTTCTCTCCTGATTTATATGAAATGACATTTTTT 600
Db 541 CATTGGTTAAAAAAACTAAAAAATAATTTCTCTCCTGATTTATATGAAATGACATTTTTT 600
Qy 601 TGGAACATGAAGGGTATTGATTTTTACCACCTTTTACACCTTTCAAAGCCATTCAAGGAT 660
Db 601 TGGAACATGAAGGGTATTGATTTTTACCACCTTTTACACCTTTCAAAGCCATTCAAGGAT 660
Qy 661 GAATATAGATTTTTGGGCGATCAAACACAAGAATCATTACGATAACATGCTTTGGAACAC 720
Db 661 GAATATAGATTTTTGGGCGATCAAACACAAGAATCATTACGATAACATGCTTTGGAACAC 720
Qy 721 ACACATGCTTAAATTAATGGTTGGAGTATCAAATTTTAAAATATTGTTGTCAATACATAC 780
Db 721 ACACATGCTTAAATTAATGGTTGGAGTATCAAATTTTAAAATATTGTTGTCAATACATAC 780
Qy 781 CCCGTCAATCTTCTTTTTTTTACCCAATAAACATTGAAATGTTGCTTCTTTCGTTAAGCA 840
Db 781 CCCGTCAATCTTCTTTTTTTTACCCAATAAACATTGAAATGTTGCTTCTTTCGTTAAGCA 840
Qy 841 TAAAAACATCAAAGTCTAGCAAAATGTTGTTTTTGCGATGACACATTTCATATAGTTTAA 900
Db 841 TAAAAACATCAAAGTCTAGCAAAATGTTGTTTTTGCGATGACACATTTCATATAGTTTAA 900
Qy 901 AGGATGCATGATTCGATTACAAAAACAAAATACTAATAATTCTAGCACAAAGTTTAAAGC 960
Db 901 AGGATGCATGATTCGATTACAAAAACAAAATACTAATAATTCTAGCACAAAGTTTAAAGC 960
Qy 961 AAGATTATAAAGCTTCATAGCATGTGGATATTCATTTAGAAATATAGATTAGATTGCCCC 1020
Db 961 AAGATTATAAAGCTTCATAGCATGTGGATATTCATTTAGAAATATAGATTAGATTGCCCC 1020
Qy 1021 TTTCATCACGGGTCTAACAGCACCACTTGTCACTACATGTCAAAAATGTCCTCTAGTACA 1080
Db 1021 TTTCATCACGGGTCTAACAGCACCACTTGTCACTACATGTCAAAAATGTCCTCTAGTACA 1080
Qy 1081 GCACCGCTTTTTACTTGATTCCCCTTGTCCATGCATGAAAAAAATCAAAACAATATTTGG 1140
Db 1081 GCACCGCTTTTTACTTGATTCCCCTTGTCCATGCATGAAAAAAATCAAAACAATATTTGG 1140
Qy 1141 ACACACAAACTTGCCCCCACTTTCCTTTTTCTTTCTGCCCTAGTTTGTTTGAGACTCATA 1200
Db 1141 ACACACAAACTTGCCCCCACTTTCCTTTTTCTTTCTGCCCTAGTTTGTTTGAGACTCATA 1200
Qy 1201 TTGATCAAATTTGGCTATGAATTCAAACAAAAAATTCACTCTACCCATTGCATGTGTGGG 1260
Db 1201 TTGATCAAATTTGGCTATGAATTCAAACAAAAAATTCACTCTACCCATTGCATGTGTGGG 1260
Qy 1261 GCCCACATATAAATCCATGAAGGATTTCAATGTCCATCCAAGTCAATGATTGACACATATA 1320
Db 1261 GCCCACATATAAATCCATGAAGGATTTCAATGTCCATCCAAGTCAATGATTGACACATATA 1320
Qy 1321 TAACATTGAATAATTTAATTCCAATTTGCAGTATTATGATTTAGATTGATTGCTGCAATA 1380
Db 1321 TAACATTGAATAATTTAATTCCAATTTGCAGTATTATGATTTAGATTGATTGCTGCAATA 1380
Qy 1381 CGGTCCGTGAATGTGATCACTCACGAGAAAGAGGTATCAAAATTTCAAGGTATTTTATTT 1440
Db 1381 CGGTCCGTGAATGTGATCACTCACGAGAAAGAGGTATCAAAATTTCAAGGTATTTTATTT 1440
Qy 1441 ATTTTTAACAAATAAAATTTCAAGGTCTTGTTCACCATATAAACCTCCTCACTCACACCC 1500
Db 1441 ATTTTTAACAAATAAAATTTCAAGGTCTTGTTCACCATATAAACCTCCTCACTCACACCC 1500
Qy 1501 AATTCTCTTAAGTGTATGACTTCATAGTACACTACACTACTTTCTTTGAAACATG 1555
Db 1501 AATTCTCTTAAGTGTATGACTTCATAGTACACTACACTACTTTCTTTGAAACATG 1555

Winicov teaches an expression cassette capable of directing heterologous protein expression in plant roots comprising an MsPRP2 promoter or a fragment thereof and "other genes" operably linked to the MsPRP2 promoter (paragraph spanning pages 19-20). The promoter or fragment thereof comprises a portion of SEQ ID NO : 1. The "other genes" are genes for a "heterologous" protein because "other" genes are not the MsPRP2 gene from which the promoter was obtained.

While Winicov does not exemplify plant and plant cell cultures transfected with the expression cassette of claim 1, Winicov teaches that such plants and plant cell cultures can be made (page 4; page 24 claims 9-11). Winicov also teaches the production of a recombinant protein in plant cells, because expression of the Alfin1 coding sequence in a sense orientation results in Alfin1 protein overexpression (page 11 last full paragraph). Winicov additionally teaches that the MsPRP2 promoter comprises the elements necessary for promoter function (Figure 3). Winicov further teaches the production of alfalfa plants transformed with expression cassettes that comprise the Alfin1 coding sequence under the control of a CaMV 35S promoter (pages 11-17). Winicov also teaches that expression of native MsPRP2 gene is enhanced in transgenic plants that overexpress Alfin1, and that the MsPrP2 promoter sequence contains Alfin1 binding sites (page 11 last full paragraph; page 8 Table 2).

Winicov does not teach explicitly teach a MsPRP2 secretion signal, or the production of a secreted protein.

Lee et al. teach the production of secreted proteins in plant cells transformed with an expression cassette comprising a promoter, a sequence encoding a secretion signal peptide, and a protein coding sequence (claims 1-17). Lee et al. also teach that secreted proteins are generally

translated as precursor polypeptides that include an N-terminal "signal sequence" or "signal peptide" that directs the transfer of the growing polypeptide chain across the membrane and into the endoplasmic reticulum for eventual secretion from the cell, and that a "signal sequence" or "signal peptide" from a secreted protein native to the cultured host plant cell, or from a secreted heterologous polypeptide obtained from another species, whether plant or mammalian or other eukaryote, can be used to target foreign polypeptides for secretion from plant cells when fused to the foreign polypeptide by conventional recombinant DNA techniques (column 5 line 50 to column 6 line 21).

Deutch C.E. et al. teach the presence of an N-terminal secretion signal in the coding sequence of the MsPRP2 gene of alfalfa (page 413 Fig. 1).

Winicov also refers at page 3 to Deutch C.E. et al. with respect to the cloning of the MsPRP2 gene from alfalfa.

Given the teachings of Winicov that plant cells can be transfected with an expression cassette comprising an MsPRP2 promoter and a protein coding sequence, and that recombinant proteins can be produced in said plant cells, given the teachings of Lee et al. that recombinant proteins can be produced in and secreted from plant cells transformed with an expression cassette comprising a promoter, a sequence encoding a secretion signal peptide, and a protein coding sequence, an expression cassette a sequence encoding a secretion signal peptide that is native or heterologous to the protein coding sequence, and given the teachings of Deutch C.E. et al. teach the coding sequence of the MsPRP2 gene of alfalfa includes an N-terminal secretion signal, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to make plant cells transfected with an expression cassette comprising an MsPRP2 promoter, a

sequence encoding a MsPRP2 secretion signal peptide, and a protein coding sequence, and to produce a secreted recombinant protein in such plant cells. One skilled in the art would have been motivated to do so in order to obtain a secreted expressed recombinant protein from the plant cells. One skilled in the art would have had a reasonable expectation of success, given that the MsPRP2 promoter comprises both the elements necessary for promoter function, given the success of Lee et al. in producing secreted expressed recombinant proteins in plant cells using heterologous secretion signal peptides, and given that the coding sequence of the MsPRP2 gene of alfalfa includes an N-terminal secretion signal.

Also, given the additional teachings of Winicov that an expression cassette comprising another promoter and an Alfin1 coding sequence can be made, that expression of native MsPRP2 gene is enhanced in transgenic plants that overexpress Alfin1, and that the MsPrP2 promoter sequence contains Alfin1 binding sites, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to make an expression cassette comprising the MsPRP2 promoter, a sequence encoding a MsPRP2 secretion signal peptide, a gene for a heterologous protein, and another promoter and an Alfin1 coding sequence. One skilled in the art would have been motivated to do so in order to increase the expression of the heterologous protein from the MsPRP2 promoter. One skilled in the art would have had a reasonable expectation of success, given the success of Winicov in making transgenic plants that overexpress Alfin1, and given that the MsPRP2 promoter comprises both the elements necessary for promoter function and contains Alfin1 binding sites.

Accordingly, one skilled in the art would have been motivated to generate the claimed invention with a reasonable expectation of success. Thus, the claimed invention would have been

*prima facie* obvious as a whole to one of ordinary skill in the art at the time the invention was made.

Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Winicov (WO 99/53016, published October 21, 1999) in view of Lee et al. (U.S. Patent No. 6,020,169, issued February 1, 2000), Deutch C.E. et al. (Post-transcriptional regulation of a salt-inducible alfalfa gene encoding a putative chimeric proline-rich cell wall protein. Plant Mol Biol. 1995 Jan;27(2):411-8) and Borisjuk N.V. et al. (Production of recombinant proteins in plant root exudates. Nat Biotechnol. 1999 May;17(5):466-9).

Claim 4 is drawn to a plant transfected with the expression cassette of claim 1.

The teachings of Winicov, Lee et al. and Deutch C.E. et al. are set forth above.

Winicov, Lee et al. and Deutch C.E. et al. do not teach a plant transfected with the expression cassette of claim 1.

Borisjuk N.V. et al. teach a method for the production of recombinant proteins in plants by genetically engineering plants to continuously secrete recombinant proteins from their roots into a hydroponic medium (page 467 Figures 1 and 2; page 468 Figure 3).

Given the teachings of Winicov that plant cells can be transfected with an expression cassette comprising an MsPRP2 promoter and a protein coding sequence, and that recombinant proteins can be produced in said plant cells, given the teachings of Lee et al. that recombinant proteins can be produced in and secreted from plant cells transformed with an expression cassette comprising a promoter, a sequence encoding a secretion signal peptide, and a protein coding sequence, an expression cassette a sequence encoding a secretion signal peptide that is native or

heterologous to the protein coding sequence, given the teachings of Deutch C.E. et al. teach the coding sequence of the MsPRP2 gene of alfalfa includes an N-terminal secretion signal, and given the teachings of Borisjuk N.V. et al. that recombinant proteins can be produced in and secreted from the roots of plants transformed with an expression cassette comprising a promoter, a sequence encoding a secretion signal peptide, and a protein coding sequence, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to make transgenic plants transfected with an expression cassette comprising an MsPRP2 promoter, a sequence encoding a MsPRP2 secretion signal peptide, and a protein coding sequence, and to produce a secreted recombinant protein in such plants. One skilled in the art would have been motivated to do so in order to obtain a secreted expressed recombinant protein from the plants. One skilled in the art would have had a reasonable expectation of success, given that the MsPRP2 promoter comprises both the elements necessary for promoter function, given the success of Lee et al. in producing secreted expressed recombinant proteins in plant cells using heterologous secretion signal peptides, given that the coding sequence of the MsPRP2 gene of alfalfa includes an N-terminal secretion signal, and given the success of Borisjuk N.V. et al. in producing transgenic plants that secrete recombinant proteins from their roots into a hydroponic medium.

Accordingly, one skilled in the art would have been motivated to generate the claimed invention with a reasonable expectation of success. Thus, the claimed invention would have been *prima facie* obvious as a whole to one of ordinary skill in the art at the time the invention was made.

Claims 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Winicov (WO 99/53016, published October 21, 1999) in view of Lee et al. (U.S. Patent No. 6,020,169, issued February 1, 2000), Deutch C.E. et al. (Post-transcriptional regulation of a salt-inducible alfalfa gene encoding a putative chimeric proline-rich cell wall protein. Plant Mol Biol. 1995 Jan;27(2):411-8) and Drake P.M. et al. (Transgenic plants expressing antibodies: a model for phytoremediation FASEB J. 2002 Dec;16(14):1855-60).

Claim 8 is drawn to seeds for plants producing a heterologous protein in its roots, the seeds comprising transgenic plant cells which have been transformed with an expression cassette comprising a promoter of MsPRP2 or a fragment thereof, nucleotides encoding a heterologous protein, and a MsPRP2 plant secretion signal operably linked thereto.

Claim 9 is drawn to a method of bioremediating a field, the method comprising planting the transgenic seeds of claim 8, wherein planting the seeds bioremediates the field.

The teachings of Winicov, Lee et al. and Deutch C.E. et al. are set forth above.

Winicov also implicitly teaches seeds because Winicov teaches seed bearing plants, e.g. alfalfa.

Winicov, Lee et al. and Deutch C.E. et al. do not teach field bioremediation.

Drake P.M. et al. teach the use of antibody expressing transgenic plants to neutralize bioactive molecules in the rhizosphere for the purpose of phytoremediation of pollutants for which it is possible to generate a monoclonal antibody (page 1855; page 1857 Figures 1 and 2; page 1859).

Given the teachings of Winicov that plant cells can be transfected with an expression cassette comprising an MsPRP2 promoter and a protein coding sequence, and that recombinant

proteins can be produced in said plant cells, given the teachings of Lee et al. that recombinant proteins can be produced in and secreted from plant cells transformed with an expression cassette comprising a promoter, a sequence encoding a secretion signal peptide, and a protein coding sequence, an expression cassette a sequence encoding a secretion signal peptide that is native or heterologous to the protein coding sequence, given the teachings of Deutch C.E. et al. teach the coding sequence of the MsPRP2 gene of alfalfa includes an N-terminal secretion signal, and given the teachings of Drake P.M. et al. that neutralizing antibodies can be produced in and secreted from the roots of plants transformed with an expression cassette comprising a promoter, a sequence encoding a secretion signal peptide, and a protein coding sequence, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to make transgenic plants transfected with an expression cassette comprising an MsPRP2 promoter, a sequence encoding a MsPRP2 secretion signal peptide, and a neutralizing antibody coding sequence, and to produce in and secrete neutralizing antibodies from the roots of such plants. One skilled in the art would have been motivated to do so in order to neutralize the effect of soil pollutants. One skilled in the art would have had a reasonable expectation of success, given that the MsPRP2 promoter comprises both the elements necessary for promoter function, given the success of Lee et al. in producing secreted expressed recombinant proteins in plant cells using heterologous secretion signal peptides, given that the coding sequence of the MsPRP2 gene of alfalfa includes an N-terminal secretion signal, and given the success of Drake P.M. et al. in producing transgenic plants that secrete neutralizing antibodies from their roots.

Accordingly, one skilled in the art would have been motivated to generate the claimed invention with a reasonable expectation of success. Thus, the claimed invention would have been

*prima facie* obvious as a whole to one of ordinary skill in the art at the time the invention was made.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3 remain rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,936,708.

Applicant's response does not address this specific ground of rejection. Accordingly, the rejection is maintained. The presence of nucleotides encoding a MsPRP2 secretion signal in Fig. 3 is also noted in view of the current claim amendments.

Applicant is advised that should claim 6 be found allowable, claim 7 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application

are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

***Remarks***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cynthia Collins/
Primary Examiner, Art Unit 1638

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